Transcriptomic Signature of Trophoblast Differentiation in a Human Embryonic Stem Cell Model.

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Public Summary:
Identification of genes involved in trophoblast differentiation is of great interest to understand the cellular and molecular mechanisms involved in placental development and is relevant clinically to fetal development, fertility, and maternal health. Herein, we investigated differentiation of human embryonic stem cells (hESCs) down the trophoblast lineage by culture with bone morphogenetic protein 4 (BMP4) over a 10 day period. Within 2 days, the stemness markers POU5F1 and NANOG were markedly down-regulated, followed temporally by the up-regulation of the trophoblast markers CDX2, KRT7, HLA-G, ID2, CGA and CGB. To understand, on a global scale, changes in the transcriptome during the differentiation of hESCs down the trophoblast lineage, a large-scale microarray analysis was performed. Through whole genome analysis, more than 3,800 genes displayed statistically significant and 2-fold or greater changes in expression during the time course. Of the genes showing the largest increases, many are involved in processes associated with trophoblast biology; however, novel genes were also identified. Some of them are mainly hypothesized to be associated with extracellular matrix remodeling (i.e. NID2), and cell migration and invasion (i.e. RAB25). Using Ingenuity Pathways Analysis to identify signaling pathways involved in trophoblast differentiation or function we discovered that many genes are involved in WNT/beta-catenin, ERK/MAPK, NFKB and calcium signaling pathways, suggesting potential roles for these families in trophoblast development. This work provides an in vitro functional genomic model to identify genes involved in trophoblast development.

Scientific Abstract:
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